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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/687,799	10/17/2003	Jessica Teeling	4086.1000-002	1801

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EXAMINER	
SCHWADRON, RONALD B	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
08/03/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/687,799	TEELING ET AL.	
	Examiner	Art Unit	
	Ron Schwadron, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-102* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,7-12,15,16,21-24,29-33,41-44,47-51,59,61-65,93* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 4-6,13,14,17-20,25-28,34-40,45,46,52-58,60,66-92 and 94-102.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :5/28/04, 9/17/04, 2/28/06, 8/30/07, 10/3/07, 12/4/08, 8/6/09.

1. Applicant's election of Group I and 2F2 in the reply filed on 2/11/08 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 4-6 (nonelected species in that the elected species of 2F2 antibody is IgG1),13,14,17-20,25-28,34-40,52-58,60,70-92,94-102 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions or species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 2/11/08.

3. Applicant's election of antibody and unlabelled in the reply filed on 11/10/08 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

4. Claims 45,46,66-69 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species , there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/10/08.

5. Claims 1-3,7-12,15,16,21-24,29-33,41-44,47-51,59,61-65,93 are under consideration.

6. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration (Inventor Teeling's residence and address). See 37 CFR 1.52(c).

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 12,15,16,21,29-33,41-43,49,50,61,64, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 U.S.P.Q.2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the applicant had possession at the time of invention of claimed invention.

The claimed antibody encompasses conservative sequence modifications of the amino acid sequences recited in the claims or sequences with sequence homology as per recited in the claims or antibodies with a single defined CDR or antibodies with fragments of the sequences recited in the claims or antibodies with undefined FR regions or antibodies with unspecified substitutions (claim 61). The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity, which is characteristic of the immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc. Natl. Acad. Sci. USA, 79(6):1979-1983, March 1982). Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. MacCallum, et al. (Journal of Molecular Biology, 1996. Vol. 262, pages 732-745) analyzed many different antibodies for

interactions with antigen and state that although CDR3 of the heavy and light chain dominate, a number of residues outside the standard CDR definitions make antigen contacts (see page 733, right column) and non- contacting residues within the CDRs coincide with residues as important in defining canonical backbone conformations (see page 735, left column). De Pascalis, et al. (Journal of Immunology, 2002. Vol. 169, pages 3076-3084) demonstrate that grafting of the CDRs into a human framework was performed by grafting CDR residues and maintaining framework residues that were deemed essential for preserving the structural integrity of the antigen binding site (see page 3079, right column). Although abbreviated CDR residues were used in the constructs, some residues in all 6 CDRs were used for the constructs (see page 3080, left column). Thus it is unpredictable as to what amino acids can be substituted into the original intact antibodies disclosed in the specification wherein the antibodies would still have the functional properties recited in the claims. Thus, the written description provided in the specification is not commensurate with the scope of the claimed inventions. In view of the aforementioned problems regarding description of the claimed invention, the specification does not provide an adequate written description of the invention claimed herein. See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1404-7 (Fed. Cir. 1997). In University of California v. Eli Lilly and Co., 39 U.S.P.Q.2d 1225 (Fed. Cir. 1995) the inventors claimed a genus of DNA species encoding insulin in different vertebrates or mammals, but had only described a single species of cDNA which encoded rat insulin. The court held that only the nucleic acids species described in the specification (i.e. nucleic acids encoding rat insulin) met the description requirement and that the inventors were not entitled to a claim encompassing a genus of nucleic acids encoding insulin from other vertebrates, mammals or humans, id. at 1240. The Federal Circuit has held that if an inventor is "unable to envision the detailed constitution of a gene so as to distinguish it from other materials. . .conception has not been achieved until reduction to practice has occurred", Amgen, Inc. v. Chugai Pharmaceutical Co, Ltd., 18 U.S.P.Q.2d 1016 (Fed. Cir. 1991). Attention is also directed to the decision of The Regents of the University of California v. Eli Lilly and Company (CAFC, July 1997) wherein is stated: The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 222 USPQ 369,

372-373 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

Thus, as we have previously held, a cDNA is not defined or described by the mere name "cDNA," even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA. See Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 9,10,29,24 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9,10,29 are indefinite in the recitation of "characteristics" because it is unclear what said term means or encompasses in the context recited in the claims. Said term is not defined the specification and has no art recognized meaning. Claim 61 is indefinite in the recitation of "derived" because it is unclear what said term means or encompasses in the context recited in the claims. Said term is not defined the specification and has no art recognized meaning.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1,2,7-11,22-24,29,44,47,48,51,59,61-63,65 are rejected under 35 U.S.C. 102(b) as being anticipated by Kucherlapti et al. (WO 96/33735) as evidenced by Teeling et al. (2006).
Kucherlapti et al. disclose human antibodies made in transgenic mice that bind to human CD20 (see abstract, page 14, claim 27, pages 5-16). The antibodies would inherently have the functional properties recited in the claims because they are made using the same method (aka using transgenic mice that produce human antibodies). Claim 2 recites all of the known isotypes of human antibodies. Antibodies produced via murine hybridomas are glycosylated. Kucherlapti et al. teach hybridomas producing said antibodies (see page 9, last paragraph, continued on next page). The recitation of a method wherein the antibody is produced carries no weight in the instant product claim. Kucherlapti et al. teach a pharmaceutical composition of said antibodies (see page 17-18) wherein the antibodies can be monoclonal or polyclonal (see pages 9-10). The composition of polyclonal antibodies would contain multiple therapeutic antibodies. Teeling et al. indicate that all human antiCD20 antibodies inherently bind the epitope recited in claims 23-24 (see abstract). The term "derived" whilst indefinite as per above will be interpreted as having any amino acid in common with the recited sequences.

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1-3,7-11,22-24,29,44,47,48,51,59,61-63,65,93 are rejected under 35 U.S.C. 103(a) as being unpatentable over Korman et al. (WO 01/14424) in view of Kucherlapti et al. (WO 96/33735).

Korman et al. teach IgG1 human antibodies made in transgenic mice that bind to a therapeutically relevant human cell surface antigen (see pages 8-9, 32-34) wherein said antibodies are made using the same transgenic mouse as per used by applicant in the specification (aka Hco7, see page 70-71). Antibodies produced via murine hybridomas are glycosylated. Korman et al. teach hybridomas producing said antibodies (see pages 32-34). Korman et al. teach a pharmaceutical composition containing one or more of said antibodies (see page 47) and additional therapeutic agents (see page 51). Korman et al. teach kits containing said antibodies (see page 65). Korman et al. do not teach that the antibody binds CD20. Kucherlapti et al. disclose that it is desireable to produce human antibodies made in transgenic mice that bind to human CD20 (see abstract). The antiCD20 antibodies made by the methods of Korman et al. would use the same transgenic mice (aka Hco7) as used in the specification, wherein said mice would produce antibodies with the same properties as those recited in the claims because the antibodies are made in the same transgenic mice. The term "derived" whilst indefinite as per above will be interpreted as having any amino acid in common with the recited sequences. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Korman et al. teach IgG1 human antibodies made in transgenic mice that bind to a therapeutically relevant human cell surface antigen and methods of making such antibodies whilst Kucherlapti et al. disclose that it is desireable to produce human antibodies made in transgenic mice that bind to human CD20. One of ordinary skill in the art would have been motivate to do the aformentioned because Kucherlapti et al. disclose that it is desireable to produce human antibodies made in transgenic mice that bind to human CD20. Furthermore, in KSR Int'l Co. v. Teleflex Inc., 550 U.S. m, 2007 WL 1237837, at "13 (2007) it was stated that **"if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill"**.

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ron Schwadron, Ph.D. whose telephone number is (571)272-0851. The examiner can normally be reached on Monday-Thursday 7:30-6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ron Schwadron/
Ron Schwadron, Ph.D.
Primary Examiner, Art Unit 1644